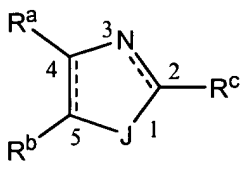
This listing of claims will replace all prior versions, and listings, of claims in the application:

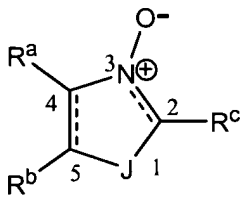
Listing of Claims:

Claim 1. (Currently Amended) A method of, in an animal, including a human, inhibiting the formation of, or reversing the preformation of, advanced glycosylation end products, thereby treating (i) diabetes or treating or ameliorating (ii) adverse sequelae of diabetes, (iii) kidney damage, (iv) damage to blood vasculature, atherosclerosis, peripheral vascular disease, coronary heart disease or heart failure, (v) hypertension, (vi) retinopathy, (vii) peripheral neuropathy, (viii) cataracts, (ix) osteoarthritis, (x) rheumatoid arthritis, (xi) Alzheimer's disease, (xii) damage to a tissue caused by contact with elevated levels of reducing sugars or (xiii) stroke, or (xiv) improving the elasticity or reducing wrinkles of the skin of an animal or (xv) increasing RBC deformability, comprising ~~inhibiting the formation of, or reversing the preformation of, advanced glycosylation end products by~~ administering an effective amount of a compound of formula I or IA,



I

or



IA

wherein:

a. J is oxygen~~,~~ or sulfur~~, or N-R^d~~;

b. the carbon 2 to nitrogen bond is a double bond except when R^c is oxo;

c. the bond between carbons 4 and 5 is a single bond or a double bond;

d. R^a and R^b are

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, allyl, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic

acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl; ~~Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar-alkyl, ArO-, $ArSO_2$-, ArSO1, ArS-, $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-~~, or together ~~R_1 and R_2~~ R^a and R^b comprise methylenedioxy-; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having up to two double bonds including a fused double bond of the containing group, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo; or

4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to eight membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2;

~~**e.** R^d is alkyl, alkenyl, hydrogen, or Ar;~~

e f. R^c is

1. oxo (when $\Delta^{2,3}$ is not present), or (when $\Delta^{2,3}$ is present) hydrogen, alkyl, alkylthio, hydrogen, mercapto, amino, amino(C_1-C_5)alkyl, amino(C_6 or C_{10})aryl, or wherein the amino of the last three groups can be substituted with

(a) Ar,

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or $-SO_2-$

(c) formyl or alkanoyl, or

(d) up to two alkyl,

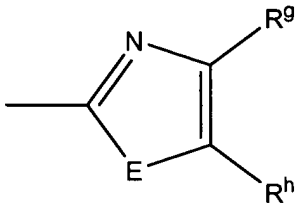
2. -NHC(O)$(CH_2)_n$-D-R^eR^f, wherein D is oxygen, sulfur or nitrogen, wherein where D is nitrogen n is 0, 1 or 2, but when D is oxygen or sulfur n=1 or 2, and R^f is present only when D is nitrogen,

wherein

(a) R^e is

(1) Ar,

(2) a group of the formula II,



II

wherein E is sulfur, oxygen, or N-R^i, and R^g, R^h and R^i are independently the same as R^a, R^b and R^d, respectively,

(3) a C_3-C_8 cycloalkyl ring having up to one double bond with the proviso that the carbon linking the cyloalkyl ring to D is saturated, which cycloalkyl ring can be substituted by one or more alkyl-, alkoxycarbonyl-, amino-, aminocarbonyl-, carboxy-, fluoro-, or oxo-substituents;

(4) a 5- or 6-membered heteroaryl ring containing at least one and up to three atoms of N for the 6-membered heteroaryl rings and from one to three atoms of N or one atom of O or S and zero to two atoms of N for the 5-membered heteroaryl rings;

(5) hydrogen, (C_2-C_6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkoxyimino), alkoxycarbonyl, a group Ar^Φ which is C_6- or C_{10}- aryl or a 5- or 6-membered, or 9- or 10-membered heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar^Φ-alkyl; and

(b) R^f is independently hydrogen, (C_2-C_6)hydroxyalkyl, alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, Ar^Φ, or Ar^Φ-alkyl;

wherein aryl, Ar, or Ar^Φ can be substituted with, in addition to any substitutions specifically

noted one or more substituents selected from the group of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C_1-C_3)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, ArO-, Ar-, Ar-alkyl-, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl-, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and

heterocycles, except those of Ar and Ar^{Φ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C_1 to C_3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl- ;

or a pharmaceutically acceptable salt of said compounds~~,~~

~~with the proviso that where the compound of formula I is administered to decrease intraocular pressure at least one compound of formula I administered in effective amount is not a thiazole substituted on a ring carbon sulfonamide (the amide of which can be substituted) that has carbonic anhydrase inhibiting activity~~.

Claims 2-3. (Withdrawn)

Claim 4. (Original) The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein J is S or O, and R^c is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with

(a) Ar;

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-; or

(c) formyl or alkanoyl.

Claim 5. (Original) The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein J is S, and R^c is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with

(a) Ar;

(b) Ar-Z-, Ar-alkyl-Z-, Ar-Z-alkyl, Ar-amino-Z-, Ar-aminoalkyl-Z-, or Ar-oxyalkyl-Z- , wherein Z is a carbonyl or -SO_2-; or

(c) formyl or alkanoyl.

Claim 6. (Original) The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein the compound is selected from the group consisting of thiazole, 2-amino-4-chlorobenzothiazole, 2,4,5-trimethylthiazole, 2-(3,5-dimethylphenoxy)-N-thiazol-2-yl)acetamide- , 2-isobutylthiazole, (4-fluorophenyl)thiazolin-2-ylamine, 2-furyl-N-[4-(6-methylbenzothiazol-2-yl)phenyl]carboxamide, and 5,5-dimethyl-2-(2-naphthylamino)-4,5,6-trihydrobenzothiazol-7-one.

Claim 7. (Currently Amended) The method of claim 1, comprising administering an effective amount of a compound of the formula I, wherein

R^a and R^b are

1. independently selected from hydrogen, acylamino, alkanoyl, alkanoylalkyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, amino, ω-alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), cycloalkyl, dialkylamino, halo, hydroxy, (C_2-C_6)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, piperazin-1-yl~~, Ar {wherein, consistent with the rules of aromaticity, Ar is C_6 or C_{10} aryl or a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a substituted benzene, pyridine, pyrimidine, pyridazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar-alkyl, ArO , $ArSO_2$-, ArSO-, ArS , $ArSO_2NH$-, ArNH, (N-Ar)(N-alkyl)N , ArC(O) , ArC(O)NH-, ArNH-C(O) , and (N-Ar)(N-alkyl)N-C(O)~~ ; or

2. together with their ring carbons form a C_6- or C_{10}- aryl fused ring; or

3. together with their ring carbons form a C_5-C_7 fused cycloalkyl ring having no double bonds except a fused double bond of the formula I or IA ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, amino, aminocarbonyl, carboxy, fluoro, or oxo, where multiple substituents are located on different carbon atoms of the cycloalkyl ring, except in the case of alkyl and fluoro substituents, which can be located on the same or different carbon atoms; or

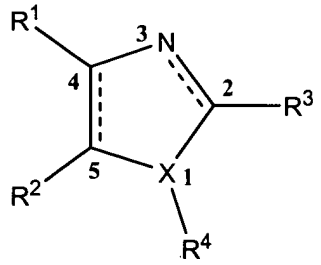
4. together with their ring carbons form a fused 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N; or

5. together with their ring carbons form a fused five to six membered second heterocycle, wherein the fused heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, oxygen, sulfur, and $S(O)_n$, wherein n is 1 or 2,

~~wherein aryl, Ar, or Ar^{Φ} can be substituted with, in addition to any substitutions specifically noted one or more substituents selected from the group of alkyl, amino, dialkylamino, 1-pyrrolidinyl, 4-[C_6 or C_{10}]arylpiperazin-1-yl, 4-[C_6 or C_{10}]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperazin-1-yl, piperidin-1-yl; and heterocycles, except those of Ar and Ar^{Φ}, can be substituted with in addition to any substitutions specifically noted one or more substituents selected from acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, (C_1 or C_3)alkylenedioxy, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, Ar-alkyl, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, oxo, sulfamoyl, trifluoromethyl, 4-[C_6 or C_{10}]arylpiperidin-1-yl and 4-[C_6 or C_{10}]arylpiperazin-1-yl, wherein multiple substituents are located on different atoms of the heterocyclic ring, with the proviso that alkyl, alkoxycarbonyl, and fluoro substituents can be substituted on the same carbon atom of the heterocyclic ring~~.

Claim 8. (Currently Amended) A method of, in an animal, including a human, inhibiting the formation of, or reversing the preformation of, advanced glycosylation end products, thereby treating (i) diabetes or treating or ameliorating (ii) adverse sequelae of diabetes, (iii) kidney damage, (iv) damage to blood vasculature, atherosclerosis, peripheral vascular disease, coronary

heart disease or heart failure, (v) hypertension, (vi) retinopathy, (vii) peripheral neuropathy, (viii) cataracts, (ix) osteoarthritis, (x) rheumatoid arthritis, (xi) Alzheimer's disease, (xii) damage to a tissue caused by contact with elevated levels of reducing sugars or (xiii) stroke, or (xiv) improving the elasticity or reducing wrinkles of the skin of an animal or (xv) increasing RBC deformability, comprising ~~inhibiting the formation of, or reversing the preformation of, advanced glycosylation end products by~~ administering an effective amount of a compound of formula III:



III

wherein:

X is ~~nitrogen or~~ sulfur~~, provided that R^4 is present only when X is nitrogen~~; the carbon 2 to nitrogen bond is a double bond except when R^3 is oxo; the bond between carbons 4 and 5 is a single bond or a double bond;

R^1 and R^2

are independently hydrogen, hydroxyalkyl, (C_2-C_6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, ~~a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,~~ or

together with their ring carbons form a C_6-C_{10} aromatic fused ring which can be substituted by one or more halo, amino, alkyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, ~~with the proviso that when X is nitrogen R^1 and R^2 do not form a C_6 fused aromatic ring,~~ or

together with their ring carbons form a C_5-C_7 fused cycloalkyl or cycloalkenyl ring having up to two double bonds including a fused double bond of the thiazole radical, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

~~R^4 is lower alkyl, lower alkenyl or Ar; and~~

R^3 is

(a) when X is S, R^3 is hydrogen, oxo, alkyl, amino, amino(C_1-C_5)alkyl or aminophenyl, wherein the amino of the latter three groups can be substituted with:

(i) Ar,

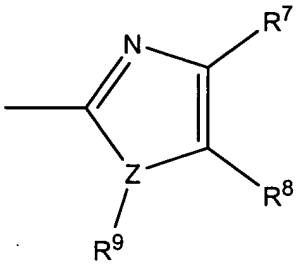
(ii) Ar-carbonyl, Ar-alkanoyl, Ar-carbonylalkyl, Ar-aminocarbonyl Ar-aminoalkanoyl or Ar-oxyalkanoyl or

(iii) formyl or alkanoyl,

(b) -$NHC(O)(CH_2)_n$-Y-R^5R^6, wherein Y is oxygen, sulfur or nitrogen, n is 0 or 1, but n=1 when Y is oxygen or sulfur, and R^6 is present only when Y is nitrogen, wherein R^5 is

(i) Ar,

(ii) a group of the formula:



IV

wherein R^7, R^8 and R^9 are independently the same as R^1, R^2 and R^4, Z is sulfur or nitrogen, R^9 is present only when Z is nitrogen;

(iii) a C_3-C_8 cycloalkyl or cycloalkenyl ring having up to one double bond, which aliphatic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups;

(iv) a 3 to 8-membered heterocyclic ring wherein the heteroatom is one oxygen, one sulfur or one nitrogen, which heterocyclic ring can be substituted by one or more amino, halo, alkyl, sulfo, sulfoalkyl, carboxy, carboxyalkyl, or oxo groups,

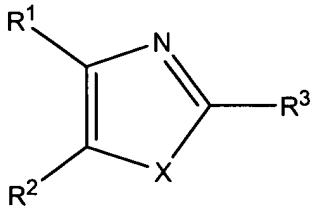
(v) hydrogen, hydroxyalkyl, (C_2-C_6)alkanoylalkyl, alkyl, alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl,

and R^6 is independently hydrogen, hydroxyalkyl, (C_2-C_6)alkanoylalkyl, alkyl,

alkoxycarbonylalkyl, alkenyl, carboxyalkyl (which alkyl can be substituted with alkyloxyimino), alkoxycarbonyl, a group Ar which is (C_6-C_{10}) aryl or (C_5-C_9) heteroaryl (wherein the heteroatom is one oxygen, one sulfur or one nitrogen) or Ar-alkyl;

wherein each group Ar can be substituted by one or more halo, amino, alkyl, alkoxy, alkoxycarbonyl, sulfo, or sulfoalkyl, groups, or a C_1-C_3 alkylenedioxy group, or a pharmaceutically acceptable salt of said compounds.

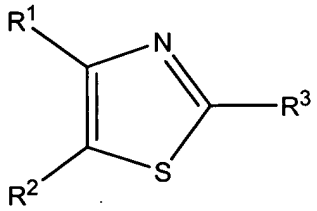
Claim 9. (Currently Amended) The method of claim 8, comprising administering an amount effective therefor of one or more compounds of the following formula:



V

wherein R^1, R^2 and R^3 are defined in claim 1.

Claim 10. (Original) The method of claim 8, comprising administering an amount effective therefor of one or more compounds of the following formula:



VI

wherein R^1, R^2 and R^3 are defined in claim 1.

Claim 11. (Original) The method of claim 8, comprising administering an amount effective therefor of one or more compounds of formula III, wherein each Ar or cycloalkyl group is substituted with up to two substituents.

Claims 12-17. (Withdrawn)

Claims 18-25. (Previously Canceled).